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ECTOPARASITISM

Canine Scabies -
1. Ivermectin - .3 mg/kg PO once weekly or .2 - .3 mg SubQ q 10 – 14 days until remission (pruritus subsides) – usually 4-6 weeks (4 week trial)*
2. Ivermectin – 0.5% alcohol based pour on (large animal product; 0.1 ml/kg or 0.5 mg/kg) applied between should blades q 2 weeks for 4 treatments.
3. Selamectin (Revolution, Pfizer) – once every 2 weeks until remission (usually 3 treatment trial) – note – some anecdotal reports or resistance to this product in highly endemic areas (e.g. Florida); use for confirmed cases (instead of trial therapies where mites not found on multiple scrapings)? Safe for herding breeds.
4. Milbemycin oxime – 2 mg/kg PO once every 7 days for 5 treatments or 2 mg/kg q 3 days for 3-4 weeks or 1 mg/kg q 2 days for 8 treatments (all have been shown to be effective). Ultimately, therapy should continue until remission (pruritus subsides). Trial period for this author is 4 weeks (if no significant benefit within this time, then scabies can be ruled out). Because of the large expense associated with this drug, usually only used in breeds for which ivermectin contraindicated (herding breeds).
5. Fipronil (Frontline Spray preferable, but must be very thorough with its use) – 6 ml/kg q 2 weeks (sponge on; safe for young or debilitated). If very young puppies, consider using only 3 ml/kg q 3 weeks. Safe for herding breeds.
6. Moxidectin – 250 mcg/kg SubQ weekly for 4 weeks
7. Amitraz dips – once weekly for 4-6 weeks
8. Lime sulfur dips (LymDyp, DVM) – once every 5 – 7 days.

Cheyletiella
Feline
1. Selamectin – once per month (in one study, resolved 15 of 15 cases)
2. Ivermectin - .3 mg/kg PO once weekly for 4-6 weeks; .2 - .3 mg/kg SubQ once every 10 – 14 days for 2 to 3 treatments
3. Lime sulfur dips – once every 5-7 days

Canine
1. Selamectin – once every other week for 3 – 4 therapies
2. Ivermectin - .3 mg/kg PO once weekly for 4-6 weeks; .2 - .3 mg/kg SubQ once every 10 – 14 days for 2-3 treatments.
3. Milbemycin oxime – 2 mg/kg once weekly for 4-6 weeks
4. Fipronil spary or “top spot” – once every other week for 3 treatments
5. Lime sulfur dips once every 5-7 days.

Rabbits
1. Selamectin – 12 mg/kg once every 4 weeks for two treatments

Feline Notedric Mange
1. Selamectin – one application resulted in resolution of 18 of 18 cases in one study.
2. Ivermectin as for cheyletiellosis
Lice in Dogs and Cats
1. Pyrethrum or pyrethroid shampoos or sprays
2. Fipronil (FrontlinePlus, Frontline Top Spot, Frontline Spray)

Canine Juvenile Onset, Generalized Demodex
Patients with generalized demodex are variably pruritic. When they are pruritic, it is mandatory to look for concurrent ectoparasites (scabies, fleas), secondary bacterial pyoderma and/or malassezia. With suspicions of intercurrent allergy (atopy), pruritus improvement is usually attempted with anti-histamines, oral omega 3/6 fatty acids and antipruritic shampoos and conditioners (i.e. oatmeal, pramoxine). Glucocorticoids are contraindicated.
Specific therapies for mites:
1. Amitraz (Mitaban) – once weekly or every other week
2. Ivermectin - 0.3 – 0.4 mg/kg PO once daily initially. Consider gradual work-up to this dosage over several days (such that if neurotoxicity noted, it will hopefully be at a lower dosage). If no significant improvement in 4-6 weeks, increase to 0.6 mg/kg PO once daily. Treat until 2 months beyond resolution. Not for use in herding breeds (e.g. Collie, Shetland sheepdog, Australian Shepherd, Old English Sheepdog, crosses). Cure rate is 60 – 85%. Idiosyncratic reactions (neurotoxicity) can be seen in other breeds (at any time during therapy). It is now possible to screen individuals for potential to develop ivermectin related, CNS toxicity. It has been noted that p-glycoprotein functions as an important component of the blood brain barrier (drug efflux pump which prevents ivermectin from accumulating in the brain). The mdr1 gene codes for this protein synthesis. Mutation of the mdr1 gene results in incomplete p-glycoprotein synthesis. Patients with this mutation are noted to accumulate excessive amounts of ivermectin in the CNS, culminating in neurotoxicity. Those that are heterozygous or homozygous for wild type do not experience toxicity. The genotype of an individual can be assessed by submitting a cheek swab sample. This test is currently being offered by Washington State University for a cost of about $60.00. More information regarding this test and the rational for its use can be obtained at www.vetmed.wsu.edu/depts-VCPL/.
3. Milbemycin oxime – because of expense, primarily intended for herding breeds or those intolerant to ivermectin. Start at 1 mg/kg/day per os. If no significant improvement within 4 weeks, increase to 2 mg/kg/day. Cure rate 60 – 85%.

Canine “Long Bodied” demodex mite (Demodex injai)
Presented as mature dogs with a focal area of seborrhea oleosa over the mid back region. Variable pruritus. Diagnosis: multiple scrapings. Therapy: aggressive antiseborrheic topical therapy (e.g. benzoyl peroxide shampoo), systemic antibiotic for secondary bacterial pyoderma and oral ivermectin as for juvenile onset demodicosis.

Feline Demodex
Demodex cati - the classic demodex mite that lives in the hair follicles and is most commonly seen in immunocompromised individuals (FIV, FeLV, uncontrolled diabetes etc) Produces focal to widespread areas of alopecia, variable degrees of pruritus, inflammation and scaling,crusting
Demodex gatoi - short bodied mite that lives on the surface of the epidermis. Affected individuals may have history of glucocorticoid administration or underlying allergies but it is uncommon to see other more serious, intercurrent immunocompromising diseases. This mite is communicable. Produces variable degrees of alopecia (without dermatitis) or alopecia and variable degrees of focal or more generalized dermatitis. Degree of pruritus is also variable.
Therapy: Both Demodex cati or Demodex gatoi have been most responsive to lime sulfur dips once every 5-7 days. Ivermectin – starting at 0.3 mg/kg PO once daily is only variably effective and selamectin (selamectin used once weekly for 6 weeks in one study) is usually not effective
UPDATE ON THE MANAGEMENT OF CANINE ATOPY

Atopy is defined as the heritable predisposition to the production of IgE (reaginic antibody) to otherwise ordinary environmental substances such as pollens, molds and house dust mites. It has been hypothesized that atopic individuals tend to produce a T helper 2 cell response to allergens. The Th2 cells produce cytokines which stimulate B cells to produce IgE. In contrast, nonatopic individuals tend to have a Th1 response to environmental allergens. These cells produce cytokines that suppress the proliferation and function of the allergy-promoting Th2 cells, thereby inhibiting IgE production. Allergen exposure is thought to occur both through the respiratory tract and through transcutaneous absorption of allergens.

With transcutaneous absorption, epidermal Langerhans cells trap and present allergen to T- lymphocytes which subsequently migrate to regional lymph nodes to culminate in the production of allergen specific IgE (and possibly IgGd) from B lymphocytes. IgE then binds to cutaneous mast cells. Subsequent exposure to allergen (e.g. cutaneous exposure) results in binding of this antigen to IgE, mast cell degranulation and the release of mediators of pruritus and inflammation (e.g. proteolytic enzymes, leukotrienes, prostaglandins, serotonin etc.). The influx of inflammatory cells results in the release of cytokines which may perpetuate inflammation for hours or days after allergen exposure. In human atopy, it is now thought that the disease may also eventually involve an autoimmune component wherein, due to molecular mimicry, IgE is sensitized to self proteins.

Incidence: Atopy is thought to affect as many as 15% of the canine population in the U.S. There is strong breed predilection (e.g. Golden retriever, Labrador retriever, Cocker spaniel, Shar pei, Dalmation, Boxer, Terriers (WHW, Yorkshire, Cairn, Scottish, Wirehaired, Boston), Pug, Irish Setter, Chihuahua, English Bulldog, Lhasa Apso, Miniature Schnauzer, German Shepherd). Although heritability has been strongly suspected for years, it has only recently been confirmed in Labrador and Golden Retrievers (Shaw S et al, AJVR 2004), prompting the recommendation that affected individuals not be used for breeding purposes.

Allergic to What?
Pollens of weeds, trees, grasses, house dust mites, molds, feathers, animal danders (cat, horse, cow), insects, storage mites (Tyrophagus putrescentiae, Leipidogyphus destructor, Acarus siro), human dander?

History and Clinical Signs:
1. Atopic symptoms generally develop between 6 months and 6-7 years of age with the peak onset between 1-3 years. We do see individuals affected as young as 2-3 months of age.
2. Although the majority of atopics initially have seasonal pruritus, their problems worsen with age and 75 - 85% of cases will become nonseasonal.
3. The primary feature of atopy is pruritus with the vast majority of other signs created as the result of this pruritus (i.e. secondary salivary staining, erythema, hyperpigmentation, lichenification, self induced alopecia). However it is now noted that there can be some degree of a primary eruption associated with atopy (erythema or a papular dermatitis) – these changes without pruritus.
4. Pruritus and lesions generally involve the periocular region, ears, feet, flanks, axilla, anterior elbow, dorsal back, perivulvar and perianal regions. Not all areas need be affected in the same dog. Pruritus and lesions are usually quite symmetrical.
5. 80% - 85% will have otitis externa. The proximal pinna (entrance to vertical canal) tends to be most characteristically involved. Secondary malassezia/bacterial infections common. In our area, underlying atopy is the most common cause of recurrent aural hematomas.

6. Secondary seborrheas (sicca or oleosa) are common.

7. Superficial (at at times, deep) bacterial infections primarily caused by Staphylococcus intermedius – common. Atopy in the dog has been noted to predispose to recurrent staphylococcal infections through a number of mechanisms:
   a. The skin of atopic dogs has been shown to allow for greater adherence of Staph. to the skin surface (promoting increased colonization and likely predisposing to infection).
   b. Atopic dogs have been noted to have abnormal immunologic responses which may predispose to infection
   c. Secondary seborrhea and self trauma may also provide microenvironments that predispose to secondary infections

Staphylococcal colonization and infection may or may not be pruritogenic in an atopic individual. They may significantly contribute to the production of pruritus through the production of pruritogenic proteases and the production of staphylococcal IgE (Staphylococcal hypersensitivity). In man, it is also noted that Staph. may produce endotoxins that serve as superantigens which may actually perpetuate the allergic response. It has also been noted that these superantigens may actually interfere with the anti-inflammatory action of glucocorticoids in the skin.

Staphylococcal infections may be very important to the clinical signs manifest in a given allergic individual (so much so, that just by controlling infections, the overall comfort of the individual will be improved very significantly). Control of the underlying allergic disease often results in a reduced tendency to develop infections in these individuals. However, there is a smaller subset of individuals who will remain prone to recurrent infections, even with control of the underlying allergy.

8. Malassezia colonization / infection – common. Some affected individuals have been noted to develop IgE mediated Type I hypersensitivity to intracellular protein extracts of *Malassezia pachydermatis*. These reactions may as well contribute significantly to the development of pruritus and inflammation. They also raise questions about the significance of Malassezia based on assessment of numbers of organisms. Where hypersensitivity reactions are involved, smaller numbers of yeast may contribute significantly to symptomatology. The above observations argue for the diligent management of secondary *Malassezia* infections to maximize comfort for our patients.

9. Hyperhidrosis (usually with more severe, chronic disease; severe inflammation of skin) – less common
10. Lick granuloma and acute moist dermatitis (“hot spots”) - uncommon
11. Conjunctivitis, rhinitis, reverse sneezing, asthma-like symptoms - uncommon
12. Anal sacculitis - uncommon
13. Lethargy, irritability, weight loss (with severe disease)
14. It is common to see concurrent flea bite hypersensitivity in atopic dogs.
15. 5 - 10% of atopics will have concurrent adverse reactions to food

**Diagnosis** - The diagnosis of atopy is accomplished largely by history, physical examination and rule out (i.e. differentiating atopy from other pruritic diseases such as flea bite hypersensitivity, scabies and food allergies). The histology of canine atopy is relatively non-specific, exhibiting an inflammatory pattern characterized as chronic, hyperplastic (thickened epidermis) and spongiotic (epidermal edema) with perivascular accumulations of lymphocytes mast cells (35% of cases?) and low numbers of eosinophils.

Intradermal testing or serologic testing for atopy are primarily performed to formulate solutions for hyposensitization. They may also provide data to allow for avoidance from some allergens. Due to
the potential for both false positives and negatives, these diagnostics should only be performed in patients who are highly suspect to be atopic.

Intradermal testing appears to provide more specific data than serologic testing (less false positives). With-drawl times for various medications prior to testing include two weeks for antihistamines, 4-6 weeks for oral glucocorticoids, 8 weeks for “dep” steroids (keeping in mind that with longer term, higher dosage therapy, with- drawl times may be much longer than these) and two to three weeks from relatively short term topical glucocorticoids. Although the author also recommends a two week with-drawl from fatty acid therapy, this point is controversial. It is important to note that “false” negative tests may occur in as many as 20 - 30% of cases. These negatives may be a product of previous medications, off season testing (testing more than two months after the end of the season) and inherent host factors (estrus, pseudopregnancy, stress). In atopics with severe clinical signs it has been suggested that anergy occurs with excessive mast cell degranulation, and that no additional degranulation can be triggered with the skin test injections, giving a false negative result. In man, it is also noted that as many as 20% of atopics will be negative on both skin tests and in vitro serologic testing. These individuals have been said to suffer from “intrinsic” atopy (vs extrinsic atopy) wherein their atopy involves an inherent abnormality in their immunologic responses which are devoid of extrinsic factor influences (allergen exposure etc).

In vitro serology is considered less specific than intradermal testing, but is still a reasonable alternative to IDT. Both false positives and/or false negatives may be a trait of any given test. Antihistamines or fatty acids need not be discontinued for this testing. With-drawl times for oral glucocorticoids are controversial and may vary with the test. In general, a two to three week with-drawl time is recommended by the author. The Heska test, however, may require an even much longer with-drawl (weeks to months). It is interesting to note that the success rates of immunotherapy based on the results of IDT compared to those obtained using serologic tests are comparable in several studies (i.e. about 60% success). Some dermatologists are routinely doing both intradermal and serologic testing and utilizing the data from both in establishing hyposensitization protocols. This approach is rationalized on the basis that the two tests measure different things. IDT measures IgE in the skin while serology measures circulating IgE and a direct correlation may not exist between the two.

Management of Recurrent Staphylococcal Infections
1. Do as much as possible to control underlying allergy
2. Treat each “flare” of pyoderma with an appropriate anti-staphylococcal antibiotic for appropriate duration of time (Clavamox, lincomycin, cephalaxin):
   a. Superficial, infrequently recurrent, localized – 3 weeks
   b. Severe, generalized, deep (even if focal) – 1-2 weeks beyond complete remission
3. Germicidal Shampoo – once weekly (Benzoyl peroxide, chlorhexidine, ethyl lactate)
   +/- Germicidal Conditioner (ResiChlor; residula chlorhexidine conditioner; Virbac) or
   +/- Antipruritic conditioner (e.g. ResiProx; pramoxine and oatmeal; Virbac)
4. Germicidal wipes / sprays
   a. Chlorhexidine and miconazole (Malaseb spray or pledgets, DVM pharmaceuticals) – once or twice daily to initiate therapy; once every 2-3 days for maintenance.
   b. Acetic acid, boric acid (Malacetic wipes; DermaPet) – used as for Malaseb above
5. Topical antibiotics – for early treatment of recurrent lesions; mupirocin (Bactoderm, Pfizer)
6. pH modulator (Advanced pHormula, Vetoquinol)
7. Patients who are very prone to recurrent bacterial infections and who derive significant benefit from systemic antibiotic therapy:
   a. Pulse cephalaxin therapy; once infection has been put in to remission with routine dosages of cephalaxin (22 – 32 m/kg BID), pulse with full dosages for 2 or 3 consecutive days of each week, whether there is infection or not)
   b. Immunomodulators
i. Staphage lysate - .5 cc twice weekly or 1 cc Sub Q once weekly for at least 4-6 month trial. Use systemic antibiotics initially to get infection under control, then discontinue to assess the benefit of the Staphage lysate. If a flare of infection noted, again treat in to remission and assess again. If recurrence of infection is not noted for a couple of months after discontinuing, begin to reduce the frequency of administration by weekly increments (looking to get to 1 cc given once monthly). If a flare of infection is noted, can transiently increase frequency of administration again.

ii. Interferon Alfa -2A (human recombinant, Intron-A, Schering), feline recombinant (Virbagen Omega, Virbac; available only in Europe and Canada at this time) or canine recombinant (available in Japan) : cytokine that has antiviral, antimicrobial, antiproliferative and immunomodulating effects. Enhancement of anti-microbial effects are thought to occur through IFNs ability to enhance macrophage activity. Low dose, daily, oral therapy (1000 units human interferon; total dose for all sized dogs) is suggested to have some benefit in reducing the incidence of infections in atopic dogs; higher dosages (10,000 U / Kg canine interferon or 1 million unites feline recombinant, three times weekly) have been noted to have some beneficial effects in reducing the signs of atopy (through altered cytokine release and decreased IgE production). Efficacy of interferons interchangeable (canine, feline, human?) E.g. Buy 5 million units/.2 mls (1.5 mls total; cost to Vet $135.00; shelf life – 6 mos to 1 year ? ); 0.1 ml in 250 ml saline (1 ml – 10,000 units); freeze in 3 ml aliquots – good for 1 year frozen?? Thaw and dilute 3 ml in 27 ml saline (1,000 U per ml). Keep refrigerated. Give 1 cc (1,000 U) per dog PO once daily. Discard after 1 month and go on to the next frozen vial. 6 month trial.

8. Patients who are very prone to recurrent Malassezia colonization/infection:
   a. Systemic therapy is often most convenient and effective. Alternatives include ketoconazole (5-10 mg/kg PO once or twice daily) for 2-4 weeks. The author generally starts at 5 mg/kg BID. Recurrences of disease can be treated with lower dosages (e.g. 5 mg/kg daily) to assess efficacy. Alternative, more expensive therapies include itraconazole (Sporanox ®, Janssen; 5 mg/kg daily for 2-4 weeks) or fluconazole (Diflucan®, Roerig; 5-10 mg/kg q 24 hrs to once weekly?). Both are less likely to have the deleterious side effects associated with ketoconazole. For patients with recurrent Malassezia, maintenance can be attempted with ketoconazole (5 mg/kg for 2 or 3 days of each week), itraconazole (5mg/kg, 2 consecutive days of the week) or fluconazole (5-10 mg/kg once weekly?).
   b. Topical therapies are less expensive, but also less effective alternatives for treating Malassezia. They are, however, valuable as adjunctive therapies to systemic drugs and as maintenance therapies once infections have been resolved. Anti-fungal, degreasing shampoos include:
      i. miconazole/chlorhexidine gluconate - Malaseb ™ (DVM)
      ii. ketoconazole/chlorhexidine- KetoChlor ™ (Virbac)
      iii. Ketoconazole - Nizoral ™ (Janssen)
      iv. Acetic acid/boric acid - Malacetic ™ (DermaPet)
      v. Chlorhexidine - Chlorhexiderm ™ (DVM); Hexadene ® (Virbac), Seba-Hex ™ (EVSCO).
These shampoos should be lathered well, left on for 5-10 min., rinsed well and repeated every 2-3 days for 2-3 weeks, then reduced in frequency of use for maintenance treatment.

c. Rinses that can be applied and left on for residual benefit (i.e. after shampoos) include:
   i. miconazole - ResiZole™ (Virbac)
   ii. chlorhexidine - ResiChlor™ (Virbac)
   iii. acetic acid and water 1:1 (white vinegar in equal parts with water).

d. Convenient topicals often added to the "between shampoo" regimens include germicidal wipes or sprays used once or twice daily:
   i. Acetic acid, boric acid - MalaAcetic Wipes™ (DermaPet)
   ii. Miconazole, chlorhexidine - Malaseb Wipes™ or spray (DVM pharmaceuticals)

Avoidance
1. With the realization of the potential importance of transcutaneous absorption of allergens, emphasis should be placed on frequent bathing (to remove allergen from the surface of the skin) and even more minor techniques such as rinsing the feet (i.e. dog with atopic pododermatitis) after spending the day in grassy/weedy environments.
2. Allergic conjunctivitis, rhinitis or periocular dermatitis - minimize exposure to airborne irritants (e.g. tobacco smoke, aerosols etc.).
3. Mold sensitivities - avoid rooms with high moisture levels (bathroom, basement); decrease numbers of house plants; use a dehumidifier.
4. Pollens - use air conditioners and air filters; avoid fields, keep lawn cut short; rinse dog after trips into grassy/weedy sights; keep dog inside when moving lawn; keep dog in early in morning and at dusk (when pollen concentrations peak).
5. House dust mite sensitivity - mites concentrated in bedding, stuffed furniture and carpets. Remove carpeting or matting, thorough regular cleaning (high efficiency vacuum). Cover mattresses with plastic; regular washing and thorough drying of bedding. Dog should not sleep on cushioned furniture and be kept in uncarpeted rooms. The documentation and semi-quantitation of house dust mite allergen concentrations are now possible through the use of technologies such as the Mite-T-Fast Allergen Detection System (AVEHO). Once detected, there is the potential for environmental mite control programs such as borate (AVEHO Dust Mite and Flea Control) and mite allergen deactivators (e.g. Allerase Anti-Allegen treatment, AVEHO).

Topical Therapies
1. **Shampoos and Conditioners:** Shampoos containing oatmeal or oatmeal and pramoxine (a local anesthetic) may give a few hours of antipruritic activity. A shampoo more recently marketed in the U.S. by Virbac (Allermyl; contains linoleic acid, L-rhamnose, Vitamine E) has performed favorably in this regard. These shampoos are usually followed up with anti-pruritic conditioners to both treat and prevent the development of dry skin which may be a product of the disease or repeated bathing. The author prefers residual conditioners for this purpose: oatmeal (ResiSoothe, Virbac), oatmeal and pramoxine (Resiprox, Virbac) or 1% hydrocortisone (ResiCort, Virbac). The hydrocortisone product appears to have superior anti-pruritic activity. In that many of our atopic patients are prone to recurrent bacterial and Malassezia infections, it is very common for us to use a germicidal shampoo (e.g. Malaseb with chlorhexidine and miconazole; DVM pharmaceuticals) on a maintenance basis. This is then followed by the use of an antipruritic conditioner (e.g. ResiProx, Virbac). The residual conditioner can also be used by itself (without shampoo) between bathings to help reduce pruritus.

2. **Topical glucocorticoids** can be very beneficial. In the past, the use of 1% hydrocortisone products have been favored by the author (e.g. CortiCalm by DVM, DermaCool-HC by Virbac or ResiCort by Virbac). More recently, a .015% triamcinolone actonide spray (Genesis Topical Spray) has been marketed by Virbac as an adjunctive therapy for allergic dermatitis. It is water-
like in consistency and odorless. In one well controlled, multi-centre study, reduction in the severity of dermatitis in allergic patients was noted in 65% of patients, versus 24% noted with a placebo (the propylene glycol vehicle). The spray is administered BID for one week, then once daily for one week, then once every other day. Absorption is minimal, but limits have been put on the amount of spray that should be administered during any given day. Polyuria was reported in 3 of 57 dogs treated and polyphagia in 1 of 57 dogs. There was no notation of the exacerbation of pyoderma in treated individuals but this should be closely monitored for. This product has proved very beneficial for better controlling the more focal manifestation of atopic pruritus. In some dogs, it has allowed for control when all other therapies have failed. Now that we have had over two years of experience with this medication, it should be noted that too frequent application over long periods of time (e.g. once every other day for 8 – 12 months) may produce significant regional hair loss, cutaneous atrophy and predisposition to local infections. Enough of the product may be absorbed to contribute to the development of generalized iatrogenic hyperadrenocorticism (e.g. widespread hair loss, cutaneous atrophy). The product must be used with respect!

3. Tacrolimus is an inhibitor of T-lymphocyte activation. It is noted to be 10 – 100 times as potent as cyclosporine. Absorption from the skin is minimal. This product has been shown to be very beneficial in the topical management of atopy in man. It is available commercially as Protopic (Fugisawa: .1%; a 30 gm tube costing about $85.00 to the client). It is initially applied BID. This product may be beneficial for the more focal, at times refractory manifestations of atopy. Its cost precludes use over large areas of the body. Tacrolimus appears to do a better job of reducing the inflammation associated with atopic dermatitis as compared to pruritus, but may work for both. This product appears to be superior to the less costly pimecrolimus (Elidel; Novartis), whose mode of activity is similar to that of tacrolimus.

Glucocorticoids
Glucocorticoids remain the most predictably effective therapies for the management of atopic pruritus and inflammation. Anti-inflammatory dosages are usually used initially (e.g. 0.5 – 1 m/kg/day of prednisone or prednisolone), with dosage tapering indicated by the severity and chronicity of skin changes, to minimize side effects and determine what the lowest dosages required to control symptoms. Glucocorticoids would be an acceptable method of management for shorter term atopic problems (e.g. 4-5 months of each year) – assuming patient tolerance. Alternatives to prednisone /prednisolone include methylprednisolone (reduce incidence of PU/PD) or Temaril-P (5 mg of trimeprazine, an antihistamine and 2 mg of prednisone per tab); may allow for lesser dosages of glucocorticoid because of the antihistamine included. Prior to considering glucocorticoids for longer term maintenance, every effort should be given to provide glucocorticoid alternatives. When this is not possible, the author will usually try to maintain the patient on the lowest, once every other day dose of Temaril-P possible. This is often facilitated by using Temaril-P along with a full, daily dose of another antihistamine such as chlorpheniramine, diphenhydramine, hydroxyzine, amitriptyline, or clemastine. This often allows one to minimize the dose of Temaril-P. Many large breed dogs may be maintained on 1-3 tabs once every other or third day. It is important, even at these low dosages to look for mild signs of iatrogenic hyperadrenocorticism (dry coat / skin; mild hair loss; gradual weight gain; increased propensity to develop bacterial pyoderma; increased propensity to develop urinary tract infections.

Fatty Acids
Although controversy still exists as to which fatty acids to use in optimizing anti-pruritic effects, products rich in n-3 fatty acids (cold water fish oils and flaxseed) appear to be favored. Using an n-3 fatty acid product (3 V Caps, DVM) at bottle dosages, significant improvement is seen in 10 - 15% of patients (10 - 90% improvement). A very small study showed superior antipruritic effects with very high dose omega 3 fatty acids (180 mg eicosapentaenoic (EPA)acid and 120 mg docosahexanoic acid (DHA) / 10
lb. body weight per day; Logas et al Vet Dermatology, 1994). A study recently completed at CSU appears to support this data. For those dogs receiving 50 – 85 mg/kg of EPA and 35 – 55 mg/kg DHA (equivalent to 1 Giant breed capsule per 5 kg body weight) or 200 – 335 mg/kg of flaxseed oil per day, 40 – 50% improved by greater than 50%. Complete remission was obtained in 10 – 20%. This suggests that higher dosages of omega 3 fatty acids should be used to initiate/assess therapy (e.g. 2-3 times the bottle dosages). Although it has been suggested that fatty acid containing products should be given at least a 12 week trial before they are critically evaluated, it was noted that most individuals had improved within the first 2-3 weeks of therapy in this study. Deleterious side effects are uncommon but include gastrointestinal upsets, increased pruritus and pancreatitis. Although high dose therapy could conceivably result in decreased neutrophil reactivity, decreased clotting and decreased wound healing, this has not been seen in clinical studies nor with clinical use.

As fat supplements, it is not uncommon for these products to improve coat luster, softness etc., even though the degree of pruritus is not reduced.

Research by Iams has shown that a 5:1 to 10:1 ratio of omega-6 to omega-3 fatty acid in the overall diet may be ideal for management of inflammatory skin disease in the dog. Their diet, formulated to meet these specifications is Eukanuba Veterinary Diets TM Response Formula FpTM for dogs. Our own uncontrolled studies evaluating the efficacy of this diet in 47 atopic dogs showed a greater than 50% reduction in pruritus in 42% of dogs.

**Antihistamines**

Antihistamines appear to benefit about 20 -30% of our atopic patients. Both first generation H1 blockers (e.g. chlorpheniramine, diphenhydramine) and second generation products that fail to cross the blood brain barrier (e.g. loratidine, ceterizine) appear to have similar success rates. It is felt that one cannot predict which, if any antihistamine, will be of help in a given individual. We generally have the owner try several different antihistamines, each for 2 weeks (3 or 4 weeks if the owner is not very observant). The owner notes which antihistamine is being used and what degree of benefit, if any, it may produce. The following are the antihistamines used most frequently in our practice. Those with an asterisk tend to be most effective/cost effective (unless otherwise marked): * Diphenhydramine (25, 50 mg caps) - 2.2 mg/kg BID or TID; * Hydroxyzine HCl (10, 50mg tabs) - 2.2 mg/kg BID or TID; * Chlorpheniramine (4, 12mg caps) .4 - .8 mg/kg (.5 mg) BID to TID; * Amitriptyline-(10, 25, 50, 75, 100 mg tabs) 2.2 mg/kg BID; * Clemastine (Tavist or generic) - 1.34 mg tabs, .05 mg/kg BID, for dogs under 10 kg 1/2 tab BID; 10 - 25 kg, 1 tab BID, bigger, 1 1/2 tab BID; Cyproheptadine - (4 mg tabs) .25 - .5 mg/kg TID; Doxepin HCl-(10, 25, 50, 75, 100, 150 mg) .5- 1.0 mg/kg BID; Trimiprazine tartrate - 2.5 - 5 mg/dog TID (expensive). Which is the most effective? Some studies have suggested clemastine; another recent study suggested hydroxyzine and diphenhydramine. The author has best results with chlorpheniramine and hydroxyzine. H 1 blockers that have antihistaminic, anticholinergic, sedative and local anesthetic effects. They must be used with caution, if at all, in the presence of liver disease, glaucoma, urinary retention, gastrointestinal atony and pregnancy.

The newer, non-sedating antihistamines include cetirizine ( 10 mg/day/animal < 25 kg and 10 mg BID > 25 kg), loratidine (0.5-1.0 mg/kg/day) and astemazole (.25 mg/kg q24hr). It has been suggested that cetirizine may be the most effective of this group. Combinations of antihistamines may be of benefit when the individual antihistamines themselves appear to have failed. The author has most commonly used chlorpheniramine along with hydroxyzine or amitriptyline or trimiprazine (in Temaril-P).

**Pentoxifylline**

Pentoxifylline (a phosphodiesterase inhibitor) has been noted to reduce the pruritus and erythema associated with atopy at a dosage of 10 mg/kg BID, although TID administration at dosages as high as 20 – 25 mg/kg may be more beneficial. The author has, in general, been disappointed with this drug as a monotherapy for atopy. It may help to reduce steroid dosages in patients on glucocorticoids, and may work synergistically with antihistamines. It is therefore usually used as part of a combination therapy,
especially when other more conventional therapies have failed. There is some suggestion that some generics may not be as effective and the trade name product (Trental). This may suggest the use of the trade name product, at least for an initial trial period of one month. If it is effective, the generic can then be tried. The author routinely uses generic products to initiate therapy.

Cyclosporine

Oral cyclosporine is now available to Veterinarians in the United States as a veterinary product (Atopica, Novartis), specifically marketed as a therapy for canine atopy. Oral cyclosporine has now been used for several years in the management of atopy in the dog. Cyclosporin-A (Neoral®, Sandoz) is most commonly used at a dose of 5mg/kg/day. It has been noted to produce good to excellent results in 70 – 80% of cases. The overall beneficial effects have been shown to be similar to those of prednisolone or methylprednisolone, without the attendant deleterious side effects of the steroid. The major side effect encountered is gastrointestinal upset (vomition, diarrhea, flatulence, abdominal cramping – with vomition being most common). The incidence of vomition may be minimized by gradually working up to the maintenance dose over several days. Cyclosporine should be given on an empty stomach (at least 2 hours before feeding) to enhance absorption. However, if vomition is noted, the drug should be stopped until this side effect has resolved and can be tried again with a small amount of food. Other side effects reported in dogs include gingival hyperplasia, papillomatosis, bacteriuria, bacterial pyoderma, anorexia, nephropathies, bone marrow suppression and a lymphoplasmacytic dermatosis. Trial therapy should be 45 - 60 days. It may take this long to see the maximal benefits of the drug. Once a beneficial effect has been noted, attempts can be made to reduce the daily dosage, or treat once every other day. It has been shown that maintenance may be achieved with either lower daily dosages or less frequent administrations. In this study (Olivry T et al, Proc. AAVD/ACVD, 2003), oral cyclosporine was reduced monthly to 2.5 and 1.25mg/kg once 50% and 75% reduction of signs were achieved. 12 of 15 dogs were able to be controlled at these dosages. In another group of dogs, a daily dose of 5mg/kg was reduced to every 2 and 4 days once patients improved by 50% and 75%, respectively. 13 of 15 individuals were able to be controlled. In yet another study of 51 dogs who were treated for 6-30 months, 15% were able to be maintained on 2-3 days per week of cyclosporine, 20% on 4-5 days per week, and 20% required daily therapy (Radowiz S et al, Proc. AAVD/ACVD 2003). It is very interesting to note that in both studies, a significant number of patients were able to have their oral cyclosporine eventually stopped, with a complete remission of disease (no recurrence) (Olivry - 10% of cases; Radowiz – 24%). In that cyclosporine is expensive, it has been used in conjunction with ketoconazole to increase the blood concentrations of the cyclosporine. The mechanism for this decrease in clearance is probably a combination of the inhibition of cytochrome P-450 in the intestine and liver and the inhibition of intestinal p-glycoprotein that would ordinarily pump oral cyclosporine into the intestine. Optimal dosages and frequencies of ketoconazole have yet to be established in atopic dogs. We tend to start with 2.5 mg/kg cyclosporine per day along with 5.0 - 10mg/kg ketoconazole once per day. A higher dose of ketoconazole (i.e. 10 mg/kg/day) may be associated with higher circulating cyclosporine concentrations and greater anti-pruritic benefits. The ketoconazole is usually given with a small amount of food, but the cyclosporine is usually given 2 hours before or after giving this small amount of food.

Behavior Component to Atopic Pruritus? - There has been a suggestion that a subset of both atopic dogs may be pruritic in response to anxiety and/or another central trigger. “These repetitive behaviors are believed to be controlled by endogenous opioid release. Dextromethorphan is an opioid antagonist that does not work by binding and blocking opioid receptors but rather by blocking receptors for N-methyl-d-aspartate, which are found in the brain and spinal cord and mediate various sensations, including pain”. Dextromethorphan has been used to significantly benefit some dogs in this fashion (2 mg/kg PO q 12 hours); in one study, 11 of 12 dogs had some degree of improvement. Dextromethorphan use should be reserved for those atopic patients that fail more traditional anti-pruritic therapy and (ideally), where there is suggestion that the behaviors are repetitive and anxiety-induced.
**Hyposensitization**

Hyposensitization is noted to benefit 60 – 70% of cases (good to excellent results). “Rush” immunotherapy, which involves giving all the induction dosages in the hyposensitizing protocol in one day appears to produce a more rapid onset of benefit from hyposensitization and possibly a higher over success rate.

Over the long term, 50 - 70% of our patients on hyposensitization require additional medication (antihistamine steroids and/or fatty acids) to control allergic signs during part or all of the year.

The majority of our patients on maintenance hyposensitization get their shots every 1-2 weeks during the allergy season. For patients who derive only transient benefits from a given shot (2-3 days), we divide our solutions and give .5 cc twice weekly, or even smaller volumes up to three times a week (e.g. .2 cc three times weekly).

It is also very important to monitor for increased pruritus following a given shot. Affected individuals may actually have their allergy signs significantly worsened if they react to the hyposensitization solution. If such is the case, we reduce the volume of solution to that which did not produce a reaction. Patients noted to have reactions to shots appear to have an overall better chance of deriving benefit from the shots, assuming the volume and frequency of solution is managed appropriately.

It is interesting to note that in one recent study (Power H et al.), 29% of patients who discontinued hyposensitization shots did so because the atopy went into spontaneous remission. We quote a 20 – 30% chance that individuals with come off hyposensitization after at least 2-3 years on the desensitizing protocol.

**UPDATE ON THE MANAGEMENT OF FELINE ATOPY**

In the older Veterinary literature, it has often been suggested that the incidence of atopy is similar to that of food sensitivity in the cat. However, in our clinic, for cats showing the clinical signs listed below, about 70% are noted to be atopic and 30% food sensitive. Feline atopy is associated with a myriad of clinical signs. These may include:

1. Alopecia with or without dermatitis due to self trauma (may be a symmetric, self – induced alopecia; higher prevalence areas tend to be the ventral abdomen, caudal thighs, dorso-medial forelimbs)
2. Pruritus directed at and restricted to the head and/or neck
3. Pruritic miliary dermatitis (lesions most commonly over the back, sides and head)
4. Eosinophilic plaques (pruritic) – most commonly over the medial thighs and ventral abdomen, but may be found over any area of the body
5. Indolent ulcer – upper lip or lips; may be the only manifestation of atopy in a given individual
6. Eosinophilic granuloma – variable pruritus; lesions may be found anywhere over the body; higher incidence in chin area, caudal thighs (linear granuloma) and oral cavity (hard and soft palate).
7. It is possible to see any of the manifestations of the eosinophilic granuloma complex (eosinophilic plaques, indolent ulcer, eosinophilic granuloma) in the same cat.
8. Recurrent or persistent otitis externa; pruritic lesions usually also noted in other areas of body, but predominant area of involvement may be the ears. Although the otitis is usually bilateral, unilateral involvement is possible. We have seen “flares” of otitis externa result in perforation of the tympana, apparently without the presence of secondary bacterial or yeast infection (pressure changes within the middle ear?).
9. Pruritic lesions may predominate in the chin and perioral region as diffuse erythema and the accumulation of dark exudates, giving the impression of feline acne; however, when clipped, classic comedo formation is not noted.
10. May exacerbate true feline acne lesions (comedoes)
11. Secondary bacterial pyoderma occurs but is less common than in the dog.
12. Secondary Malassezia infections are noted, but are less common than in the dog. They tend to predominate in the facial (folds, lip margins, chin) and foot areas (interdigital).
13. Rhinitis, conjunctivitis
14. Asthma

Feline atopy may begin as either a seasonal or non-seasonal problem. Seasonal presentations may progress to year round manifestations with time.

Feline atopy is largely diagnosed by rule out. The major differential diagnoses to be considered include flea bite hypersensitivity, food sensitivity, cheyletiella, demodicosis and dermatophytosis. It is not uncommon to see a peripheral eosinophilia and basophilia. Skin biopsies show inflammatory changes that not uncommonly reveal increased numbers of mast cells and eosinophils. The documentation of offending allergens is achieved either with intradermal skin testing, which tends to be more difficult to read than in the dog and in vitro, serologic testing. At present both RAST and ELISA tests are available for use in the cat. In one study, there was poor correlation between IDST and commercial ELISA data. In another study, similar success to hyposensitization was seen based on ELISA or IDT data. Further comments regarding the efficacy of this type of testing awaits controlled studies but it is important to note that many Veterinary Dermatologists have migrated to doing serologic testing in the cat as their choice diagnostic for defining offending allergens. This likely has most to do with its ease of performance compared to doing skin tests. It is important to note that, because of the potential for false positive results, this type of testing should not be done to diagnose atopy in the cat.

**Therapy**

The therapy of feline atopy should always include the documentation and treatment of secondary bacterial or Malassezia infections. These are best defined by cytologic examination.

Because glucocorticoids are well tolerated in the cat, they tend to be the cornerstone of therapy. However, as the disease becomes more chronic and severe, it is not uncommon to have the patient require higher dosages, more frequent dosage administrations or more potent glucocorticoids to maintain comfort. We are of the impression that prednisolone tends to be more effective than equal dosages of prednisone in some cats, and for this reason, in choosing between these drugs, we would choose to routinely use prednisolone in cats. Cats are often started on 1 – 2 mg/kg/day of prednisolone. “Depo” steroids are acceptable for periodic administration (ideally keep frequency of administration to less than once every 6-8 weeks - methylprednisolone acetate or triamcinolone acetonide). For patients refractory to prednisolone consideration should be given to using the longer acting, more potent oral dexamethasone (.1 - .2 m/kg/day) or triacginolone acetonide (.5 – 1 mg/kg/day). Emphasis should always be placed on reducing dosages to the least frequent administration possible.

Fatty acids (omega 3 and 6) such as DVM Derm Caps Liquid or 3V caps (omega 3) benefit approximately 20 - 30% of cases (some quote 30 – 50%). Many cats, however, refuse to eat the fatty acids.

The antihistamines that have been of most benefit for in our hands for treating feline atopy are chlorpheniramine (2-4 mg/cat q 12 hrs) or amitriptyline (5-10 mg/cat q 12 - 24 hrs. Amitriptyline may cause significant sedation, ataxia etc.; cats may salivate excessively when it is given. The later can be circumvented by using amitriptyline powder mixed in fish/cod liver oil. Other antihistamines to be tried include clemastine fumarate (.34 - .68 mg/cat BID), ceterizine (.5 – 1 mg/kg or 5 mg/cat) or cyproheptadine (2 mg/cat BID; may cause polyphagia and behavioral effects). Each is tried for 3 weeks.

Hyposensitization has been reported to benefit anywhere from 45% to 75% of cases. Our success rate has been in the 60 -70% range. Protocols using aqueous allegens are similar to those used for the dog. The author uses the same frequency of administration, but only 1/2 the volumes. One recently published study reported the benefits of hyposensitized based on RAST data. The numbers of patients with various
manifestations of atopy and the percentage of patients who improve by greater than 50% included: hair loss – 29 cats/53%; military dermatitis – 23 cats/76%; eosinophilic plaque – 10 cats/73%; indolent ulcer – 6 cats/95%; linear granuloma – 3 cats/100%; otitis externa – 4 cats/65%; Asthma – 4 cats/90%

Oral cyclosporine has been noted to work well in the management of atopic dermatitis in the cat. Cats are generally treated with 5 – 7 1/2 mg/kg/day. In one study, eosinophilic plaques and eosinophilic granulomas were put in to remission within 30 - 60 days. 3 cats with indolent ulcers had only partial responses. Cyclosporin at this dosage appears to be tolerated reasonably well. GI upsets (nausea, vomiting, anorhexia) are relatively common. If possible, we gradually increase our dosages over several days, prior to getting to our maintenance dose (above). If GI problems are encountered, the drug is stopped until the signs have abated and it is then re-instituted … given with a small amount of food. We have seen apparently latent toxoplasmosis exacerbated while on this therapy (likely because of the immunosuppressive effect of cyclosporine .. something to be aware of!

Chlorambucil has also been of benefit (usually along with steroids) in treating refractory atopy. Recommended dose is 0.1 - 0.2 mg/kg q 24 hrs until 75% improvement in clinical signs, then this dose every other day. Adverse effects to be monitored for include hepatotoxicity and bone marrow suppression.

Megestrol acetate may be considered a "last ditch" alternative for treating feline atopy, in light of potential side effects (polyphagia / weight gain, PU/PD, personality and behavioral changes, pyometra or stump pyometra, mammary hyperplasia, mammary neoplasia, diabetes mellitus and adrenal suppression). Remission of clinical signs can often be achieved with an oral dose of 2.5 - 5.0 mg/cat every 48 hours for 1-3 weeks. This is followed by weekly maintenance dosages.

**CANINE AND FELINE FOOD SENSITIVITIES**

Adverse reactions to foods are generally divided into various subsets based on pathomechanism. Those that are of most significance from a dermatology point of view include food intolerance and food allergy. Food intolerances mimic food allergies, but can occur on first exposure to a dietary ingredient and involve non-immunologic mechanisms. They may be further subdivided into food idiosyncrasy and pharmacologic reactions to foods. Idiosyncratic reactions to various ingredients in foods are often described in human beings. Sulfites, monosodium glutamate, tartrazine, azo and noazo dyes, benzoates, parabens and spices have all been incriminated. In the case of azo or nonazo dyes, the mechanism may involve histamine release from leukocytes. Similar reactions are suspected to occur in dogs and cats but are poorly documented. Food ingredients may also be associated with the pharmacologic action of various ingredients in foods (i.e. vasoactive amines such as histamine which can increase in spoiled scombroid fish such as tuna, mackerel, skipjack and bonito). Food allergies are immunologically mediated reactions to water soluble glycoproteins that have molecular weights ranging from 10,000 – 60,000 daltons. This data comes largely from experiences with food sensitivities in man, but appear to be applicable to the dog and cat.

**CANINE ADVERSE REACTIONS TO FOODS**

Allergic to what? In the dog, adverse reactions to beef, dairy products and wheat account for 2/3 of the reported cases. Reactions to chicken, chicken egg, lamb or soy account for another 25%. Other glycoproteins that have been incriminated include corn, oatmeal, pasta, pork, fish, turkey, potatoes, rabbit, rice flour, rice, artificial food additives (gum carrageenan) and food preservatives. In one study of 25 food allergic dogs, 80% of affected dogs were reactive to 1 or 2 allergens in the diet. 64% were sensitive to two or more allergens. The mean number of allergens reacted to was 2.4.
**Incidence:** controversial: 3-10% of all canine allergic hypersensitivity (excluding parasitic allergy). Concurrent flea bite hypersensitivity or atopy may occur in up to 75% of cases.

**Clinical Signs:** In the dog, no age or sex predilections are noted, although many cases tend to occur in younger dogs (33% - 52% less than 1 year of age in reports from various studies). The index of suspicion for food hypersensitivity is above that of atopic disease when pruritus occurs in dogs under six months of age. Breeds predisposed include American cocker spaniel, English Springer spaniel, Labrador retriever, collies, miniature schnauzer, Chinese Shar pei, poodle, west highland white terrier, Wheaten terrier, Boxer, dachshund, Dalmation, Ihasa apso, German shepherd and Golden retriever.

Pruritus is nonseasonal, although it may wax and wane if exposure to the offending allergen is episodic. Secondary seborrheic, bacterial and Malassezia problems are common. Symptoms may be restricted to just an otitis externa in as many as 20-25% of cases. Food colorants and other additives have been suggested to cause erythema multiforme and other “drug-like” skin eruptions. Lesions include erythematous macules, and papules that spread to produce annular target and arciform lesions. Involvement of the oral and nasal mucosa, pinnae, axilla and groin are common. Other associations include recurrent bacterial pyoderma (with or without pruritus), eosinophilic vasculitis (presenting as urticaria or any of the various lesions associated with vasculitis), malaise, dullness and rarely seizures. Gastrointestinal signs (vomiting, diarrhea, colic) are noted in 10-15%. Gastrointestinal signs may be characterized by only an increased frequency of bowel movements.

**Diagnosis and Therapy:** The histologic changes associated with food sensitivity in the dog are relatively nonspecific and consist of a superficial perivascular dermatitis with mononuclear cells or neutrophils predominating. Increased eosinophils are occasionally present. There is one report which suggests that the presence of eosinophilic infiltrates is more closely associated with a diagnosis of food sensitivity than atopy in the dog (when evaluated in a flea free environment). Serologic testing for food allergies (radioallergosorbent RAST or ELISA testing) and intradermal skin testing have shown poor predicatability and poor correlation with response to provocative challenge and are not recommended for diagnostic purposes.

Home prepared diets appear to be closest to 100% effective in determining the presence of food sensitivity. There are several reports in the literature of both dogs and cats who have manifest signs of food sensitivity when fed a commercial diet consisting of the same ingredients offered in a home prepared form. Home prepared diets that the author favors include a single, novel carbohydrate (potato, yams, pinto bean) combined with a single, novel protein (venison, duck, rabbit, ostrich, kangaroo). We generally feed one cup per ten pounds body weight of the mix per day; _-_ 1/3 of this mix is usually the protein component. It is recognized that these diets are nutritionally inadequate for growth and maintenance. Homemade foods lack a source of calcium, essential fatty acids, certain vitamins and various micronutrients. These homemade diets are not recommended for trial purposes in growing animals for any longer than three weeks unless they have been balanced with a non-flavored, additive free vitamin, calcium/phosphorous and a source of essential fatty acids such as vegetable oil. Vegetable oils are not likely to contribute to allergic symptoms. Because of the inconvenience factor required in home formulating balanced diets, the author tends to use commercial restrictive diets for most growing animals.

Commercial diets currently available are quite good, but it is well known that no commercial diet works for all food allergic individuals. An estimate of about an 80% - 85% chance of success with any given diet seems reasonable based on data available to date. Commercial restrictive diets can generally be divided into two categories:

a. Novel protein diets: e.g. Innovative Veterinary Diets duck, venison, rabbit and lamb and potato, Iams Eukanuba Veterinary Diets Response Formula FP (fish and potato; has additional omega 3 fatty acids which have been noted to benefit about 40% of atopic dogs; this must be taken into consideration when interpreting response), Iams Eukanuba Veterinary Diets Response Formula KO (kangaroo and
b. Protein hydrolysates: it is known in man that major food allergens are typically large glycoproteins of molecular weight greater than 12,000 Daltons. Hydrolysate diets have had their proteins chopped into smaller peptides which theoretically render them less allergenic. Some diets contain only hydrolyzed protein sources, while others contain both hydrolyzed and intact protein sources. Examples include Purina HA (hydrolyzed soy protein, corn starch), Hills Prescription diet z/d Ultra Allergen Free (starch, hydrolyzed chicken liver, hydrolyzed chicken), Prescription diet canine z/d low allergen (potato, hydrolyzed chicken liver, hydrolyzed chicken), DVM Exclude (novel carbohydrate is pinto beans ad oats, hydrolyzed protein is casein and chicken liver). Some data is available on the efficacy of these diets. In one recent study (Rosser ER, Proc. AAVD/ACVD 2001), 18 of 19 proven food sensitive dogs (specific offending allergens not specified) fed the DVM Exclude diet failed to show any exacerbation of pruritus. In another study, 21 of 23 proven food allergic dogs (allergens not specified) were noted to respond to the Purina HA diet. In our own studies, 13 food allergic dogs were fed the z/d ultra allergen free diet and none had an exacerbation of pruritus. Only recently has data been generated on the efficacy of one of these diets when fed to individuals known to be allergic to the protein in the diet (Purina Veterinary Diet HA Formula; Beale, DM, Proc. AAVD/ACVD, 2001). In this study of 10 dogs with corn or soy sensitivities or both, pruritus was reduced 50% (in soy allergic dogs = 6) to 80% (in corn allergic dogs =4) compared to dogs fed intact corn or soy. It would appear that, even in corn and soy sensitive individuals, pruritus and erythema could be expected to improve significantly on the diet, but not necessarily resolve. This would suggest that these diets may also not be "perfect" in their ability to totally assess or treat food sensitive individuals. If a partial response is noted to a hydrolysate diet, before working the dog up for other allergy types to explain the residual pruritus, it may be prudent to switch to a home prepared diet or another restrictive diet to complete the diet trial.

c. At this time, the answer to the question, "which is the best commercial restrictive diet" remains open for debate. Until more data is available on clinical trials using the hydrolysate diets, it is probably best to continue to state that there is no commercial diet that will work for all food sensitive individuals. When food sensitivity remains a possibility following the use of a commercial diet trial (i.e. diagnostics or therapies for atopy do not appear to be benefiting the skin disease), then strong consideration should be given to trying a home prepared restrictive diet to better rule out a food sensitivity component to the problem.

Diet trial duration is generally 8 weeks. Complete resolution of signs may require 10 to 13 weeks. Every effort must be made to keep the diet trial strict (no other foods, treats, flavored chew toys, flavored heartworm preventative etc.). Patients are ideally re-checked 1-2 times during the diet trial to assure compliance and examine for the presence secondary infections etc. that may complicate interpretation of the diet. Compliance may be enhanced by having the owners maintain a daily log of “degree of pruritus” and amount/types of food fed. If a response to the diet is noted, the diet should be continued until maximal benefit is achieved. A partial response (e.g. 50%) may suggest the presence of intercurrent causes of pruritus (e.g. atopy) unless the diet trial is with a hydrolysate (see above under hydrolysate diets). It is very important that potentially pruritic pyoderma and/or Malassezia infections be cleared up and controlled, early in the trial diet. It is not uncommon to continue antibiotic therapy or Malassezia topical treatment throughout the diet trial to prevent exacerbation of infection during the trial. The effect of the diet is confirmed by challenge (with the previous diet). Exacerbations of pruritus are generally noted within the first week, but may take as long as 10 – 14 days. In the event of an exacerbation of signs, re-institution of the restrictive diet usually produces a more prompt response than is encountered during the trialing period. If there is a desire to define the source of the allergy, then single protein sources can be added in to the basal diet at a frequency of one every 10 – 14 days. This data may allow for the selection of other commercial diets that can be fed in the future.
The signs associated with food sensitivities are variably responsive to glucocorticoids (some may be resistant to anti-inflammatory dosages; some may be very responsive to even low dosages). Antihistamine therapy appears to be less successful when compared to treating atopy in the dog.

FELINE ADVERSE REACTIONS TO FOODS

Allergic to What? Adverse reactions to beef, dairy products (milk, cheese) and fish have accounted for nearly 90% of the reported cases in cats. Others include pork, chicken, rabbit, horse meat, lamb, eggs, cam juice and cod liver oil.

Incidence: In one group of 25 allergic cats, flea bite hypersensitivity was seen in 70%, food sensitivity in 17% and atopy in 13%. In our practice, we feel that food sensitivity and atopy are of about equal incidence. Siamese or Siamese crosses may be at increased risk.

Clinical Signs: Pruritus is present in 100% of cases. Pruritus most commonly affects the face, head, pinnae and neck or combinations thereof. Pruritus may also be generalized or restricted to other areas of the body (e.g. racing stripe down the back). Other manifestations include self induced alopecia, military dermatitis and any of the manifestations of the eosinophilic granuloma complex (indolent ulcer, eosinophilic plaque, eosinophilic granuloma). There are rare reports of an exfoliative dermatitis characterized histologically by a lymphocytic mural folliculitis and an erythematous papulopustular eruption characterized by eosinophilic folliculitis and furunculosis related to food sensitivities in the cat. Angioedema, urticaria and conjunctivitis, sneezing, malaise, dullness and a peripheral lymphadenopathy have also been noted. Gastrointestinal signs (vomition, diarrhea) are noted in 10 – 15% of cases. Up to 25% of cases have concurrent hypersensitivities (atopy or flea bite hypersensitivity).

Diagnosis and Therapy: The histopathology of food sensitivity most commonly involves a superficial and/or deep perivascular dermatitis wherein eosinophils are the dominant inflammatory cell type. Mast cells are commonly increased and may be the prominent cell type noted. A peripheral eosinophilia may be seen in as many as 50% of cases. The diagnosis is confirmed by assessing response to a restrictive diet. Home prepared diets are again most predictably effective. Single, novel protein sources include lamb or ham baby food, ham, ostrich, rabbit, venison, duck. The protein source may be fed alone or blended with potato or rice. For the purposes of a diet trial (8 weeks), balancing the diet may not be necessary. For long term feeding, however, supplementation with taurine tablets, dicalcium phosphate, safflower oil and a multiple vitamin is recommended. Alternatively, commercial restrictive diets may also be fed. As for the dog, no commercial diet will likely be beneficial for all food allergic cats. Novel protein diets such as the Innovative Veterinary Diets (lamb, rabbit, duck, venison) are used by the author. They have the advantage of coming as both dry and canned foods to help satisfy picky appetites. Hydrolysate diets are also available (Prescription Diet Feline a/d low allergen (rice, hydrolyzed chicken liver, hydrolyzed chicken).

Cats with food sensitivities are noted to be variably responsive to glucocorticoids (50% may not respond). Response to antihistamines also appears to be generally poor.
SUNDRE CANINE PRURITIC DERMATOSES THAT MAY MIMIC ATOPY

CANINE EPITHELIOTROPIC LYMPHOMA (mycosis fungoides) – myriad of clinical presentations – considered a great mimicker: generalized pruritic erythroderma with variable degrees of scaling; depigmentation of planum nasale and/or mucocutaneous junctions; focal patches of inflammation and scaling; focal plaque or nodule formation; stomatitis. Usually seen in old dogs. Diagnosis by biopsy (suggested by cytologic examination of impression smears or aspirates of the skin). Therapies are largely palliative but may keep the patient comfortable for many months, if not a year or two.

Therapies:
1. Prednisone
2. Combinations of prednisone, chlorambucil, vincristine, cyclophosphamide, doxorubicin, methotrexate
3. Topical mechlorethamine (nitrogen mustard)
4. Retinoids (isotretinoin)
5. Interferon
6. Lomustine (CCNU) – (oral therapy, relatively well tolerated, current therapy of choice in our clinic)

SUNDRE FELINE DERMATOSES THAT MAY MIMIC FELINE ATOPY

Other differential diagnoses for feline symmetrical alopecia – due to self trauma
1. Flea bite hypersensitivity
2. Food sensitivity
3. Atopy
4. demodicosis (demodex gatoi)
5. Cheyletiellosis
6. Dermatophytosis
7. Hyperthyroidism
8. Underlying sources of irritation – cystitis, anal sacculitis
9. Psychogenic
   a. chlomipramine – 1.25 – 2.5 mg/ca/day
   b. amitriptyline – 2.5 – 5mg/cat q 12 to 24 hours (start at 2.5 mg/cat once per day in the evening and work up).

Pruritus must be differentiated from an individual who is just loosing hair (with the latter being much less common).
Several techniques may be used to help determine the mechanism of hair loss:
History - overgrooming, regurgitation of hair
Direct examination - short, stubby haircoat; normal resistance to epilation
Microscopic examination - distal hairshaft broken, some follicles in anagen, ectoparasites (e.g. Cheyletiella eggs)
Fecal examination - excess hair in feces
Trial Elizabethan collar or sweater - hair regrowth over 4-6 weeks if hair loss due to pruritus

Pruritus vs Psychogenic?
In that pruritic causes of hair loss are much more common than psychogenic causes, we emphasize elimination of all the potential causes of pruritus in the cat before returning to a tentative diagnosis of psychogenic dermatitis. Techniques used to differentiate pruritic from psychogenic causes of alopecia:
a. History
b. Trial glucocorticoids - hypersensitivity causes of pruritus usually respond, whereas psychogenic causes should not
c. CBC - hypersensitivity disorders may show eosinophilia, basophilia - psychogenic disorders will not.
d. Skin biopsies – usually not of much help unless very strongly suggestive of hypersensitivity disorder
(presence of increased mast cells +/- eosinophils). The presence of a low grade, perivascular dermatitis
(primarily lymphocytic) can be seen in normal cats, allergic or psychogenic cats.

PSYCHOGENIC ALOPECIA
Alopecia +/- dermatitis due to behavioral problems are quite uncommon in the cat as a sole cause of
alopecia due to self trauma. It is difficult to estimate how many cats with primary pruritic disease develop
a stereotypic component to their overgrooming (5 - 10%?). Cats with alopecia due to self trauma are often
considered to have anxiety neuroses caused by such things as changes in the cats environment (new
family member, new cat or dog in the house or neighborhood). Historical features that may suggest a
psychogenic etiology:

- Breed - oriental breeds predisposed
- Lifestyle - any cat faced with territorial or psychologic stress - rival or aggressive
  companions, a new baby or pet in the household, a move to new
  surroundings, the loss of a close companion
- Individual character - nervous, introverted, shy, or socially inferior cats

Cat bites/chews/pulls hair out without causing trauma to the skin. Alopecia is usually noted in easy to get
to areas: medial thighs, inguinal region caudal abdomen, anteromedial and ventromedial aspect of the
forelimbs, dorsal mid back area (racing stripe). Self trauma is often inflicted when owners not around
(closet chewers).

Workup: should include a thorough examination looking for underlying irritative problems, skin
scrapings, Wood's lamp examination, fungal culture, fecal floatation, +/- CBC (looking for an
eosinophilia which would support hypersensitivity as the cause of the problem), +/- skin biopsy (looking
for inflammatory changes that may support the presence of a hypersensitivity problem), +/- T4.

Treatment:
1. **If problem not severe, live with it?**
2. If possible, remove underlying cause.
3. If obvious psychogenic stress implicated but cannot be removed, consider 4-6 week trial with
   a behavior modifying drug:

   a. Amitriptyline – 2.5 - 5 mg/cat PO started once daily (usually at night), then go to this dose BID;
      response to therapy usually seen within 7-10 days, but may take up to a month. Side effects
      include tachycardia, urine retention, constipation, inappetence).
   b. buspirone - 2.5-5.0 mg/cat BID or TID. Expensive. Side effects uncommon but do include
      agression, hyperactivity and GI symptoms.
   c. diazepam - 0.25 - 2.5 mg/kg BID (some use 1-2 mg/cat q 12 - 24 hrs); usually response in 2-4
      weeks. Long term maintenance: 1 mg BID. Side effects: sedation, appetite stimulant, ataxia,
      idiosyncratic, fatal hepatic necrosis (within 8 - 14 days of starting treatment; monitor liver
      enzymes before and 3-5 days after initiation of therapy)
   d. clomiprimine - 0.5 mg/kg (1.25 – 2.5 mg) q 24 hrs. 1 month trial. Side effects include urine
      retention, inappetence and depression
   e. phenobarbital - 1.0 - 6.6 mg/kg BID (2 mg/kg BID); response in 2-4 weeks
   f. megestrol acetate - 2.5 - 5.0 mg total dose every other day until regrowth, then every 3 - 14 days
      as necessary or 2.5 - 5.0 mg total once daily for 5-7 days, then twice weekly (side effects -
      polyphagia, PU/PD, benign mammary hypertrophy with possible progression to mammary
      adenocarcinoma, pyometra, diabetes mellitus and adrenocortical suppression.
g. fluoxetine (Prozac) - 0.5 - 1 mg/kg PO q 24 hrs - 1 month trial
h. Naltrexone (Trexan) - 5 - 10 mg/cat/12-24 hrs

Note: If responds to one of these psychoactive therapies, but the problem is recurrent, workup for allergies before committing to long term psychoactive drug therapy for control (just in case an allergy).

If no obvious psychogenic stress, consider workup for allergies first (trial steroid regimen: 2 mg/kg/day prednisolone for 1 week, then 1 mg/kg/day for 1-2 weeks; hypoallergenic food trial, skin testing), then trial psychoactive drug therapy if this fails.

**FELINE ALOPECIA UNASSOCIATED WITH SELF TRAUMA**

a. Dermatophytosis
b. Demodicosis
c. Hyperadrenocorticism (spontaneous or iatrogenic)
d. Hypothyroidism
e. Severe, debilitating diseases (e.g. uncontrolled diabetes mellitus, end stage renal disease, severe liver disease)
f. Drug eruption
g. Telogen defluxion/anagen defluxion
h. Alopecia areata
i. Epitheliotropic lymphoma
j. Alopecia mucinosa
k. Paraneoplastic alopecia
l. Feline endocrine alopecia (sex hormone imbalance?)
m. Trichorrhexis nodosa (trauma +/- inherent weakness of hair)

**Feline Hyperadrenocorticism (Spontaneous)**
The predominant feline cutaneous changes associated with hyperadrenocorticism included (25 cases):

a. increased incidence of bruising of the skin - 40% (10/25)
b. recurrent cutaneous abscessation - 40% (10/25)
c. Truncal, flank, and/or ventral partial to complete alopecia without erythema - 88% (22/25)
d. Atrophic thin skin with prominent vasculature - 68% (17/25)
e. comedones - 16% (4/25)
f. hyperpigmentation - 12% (3/25)
g. extreme fragility of the skin - 48% (12/25) It is interesting to note that this fragility may at times be noted when alopecia is minor

The most common systemic clinical signs associated with feline hyperadrenocorticism are polydipsia, polyuria, polyphagia, lethargy, abdominal enlargement or "pot-belly", panting, obesity, muscle weakness and diabetes mellitus. Overt diabetes mellitus may result from the insulin antagonism caused by hypercortisolemia in about 85% of cats with hyperadrenocorticism. Conversely, hyperadrenocorticism can be a cause of insulin resistance and poor glycemic control in diabetic animals.

Serum chemistry abnormalities include increased serum activities of alkaline phosphatase (although less common and much less severe as compared to the dog), ALT, hypercholesterolemia, hyperglycemia and hypokalemia (especially if concurrently diabetic).
Paraneoplastic Alopecia and Internal Malignancies in the Cat
Cats with pancreatic adenocarcinoma or bile duct carcinomas may present with a symmetric alopecia involving the ventrum and extremities. Hairs are usually readily epilated. The footpads, footpad/skin junctions may be dry and scaly/crusty and occasionally fissured and painful. The alopecic skin is often smooth and "glistening" and occasionally mildly scaly and erythematous. Pruritus is usually absent. All cats manifest varying degrees of weight loss, inappetence and lethargy. Diagnosis is by skin biopsy (severe follicular and adnexal atrophy with follicular miniaturization and mild perivascular inflammation) and workup to document visceral neoplasia. The prognosis is grave.

FELINE ATOPY MIMICKERS:
IDIOPATHIC ULCERATIVE DERMATITIS OF THE SHOULDER AREA
Lesions are focal, usually singular, intensely pruritic, erosive to ulcerative and most commonly located over the dorsal interscapular region. Lesions will resolve if protected (e.g. e-collar). Histopathologic findings are nonspecific. Response to antibiotics, glucocorticoids and psychoactive drugs (e.g. clomipramine) is poor. More recently, dramatic responses have been noted to oral cyclosporine (beginning at 5 mg/kg/day).